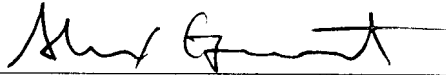


**CERTIFICATE OF USPTO ELECTRONIC FILING SYSTEM SUBMISSION**

I hereby certify that this correspondence is being transmitted herewith via the USPTO's Electronic Filing System (EFS-Web) on the date indicated below and is addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

**Date of Submission: January 8, 2008**



**Alex Grant**

Attorney Docket: 13395.1005  
PATENT APPLICATION

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: **Alicia Jennifer Hafeeza EL HAJ and Jon Paul DOBSON**

Group Art Unit: 1647

Application No. : 10/518,956

Filed : August 10, 2005

For : **METHOD OF MAGNETICALLY MANIPULATING A CELL WITH  
MAGNETIZABLE PARTICLES**

Examiner : Ian D. Dang

**DECLARATION OF PROFESSOR ALICIA EL HAJ**

COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, VA 22313-1450

The undersigned, Dr. Alicia Jennifer Hafeeza EL HAJ, hereby declares:

1. I am Professor of Cell Engineering and Director of the Institute for Science and Technology in Medicine at Keele University, the assignee of the subject patent application, and an inventor of the subject matter disclosed and claimed in the application. I have a Ph.D. in the field of bioengineering and am the author of over 100 articles in peer-reviewed journals.

2. The following studies were carried out under my direct supervision  
Exhibit A shows the results of an experiment in which magnetic nanoparticles were bound to the TREK channels in human mesenchymal stem cells via an anti-TREK antibody and activated remotely with time-varying magnetic fields for 1 hour per day for three weeks. This resulted in up-regulation of the gene, osteopontin, a key matrix component of cartilage production.  
  
Exhibit B shows the results of an experiment in which human mesenchymal stem cells in chitosan/alginate capsules were implanted subcutaneously in nude (immuno-compromised) mice. Control groups had no magnetic activation. Active groups had magnetic nanoparticles bound to the cells via an anti-TREK antibody which was activated with time-varying magnetic fields for 1 hour per day for three weeks. This resulted in the production of cartilage in this group as evidenced by the histological staining for cartilage matrix proteins in the figure. This demonstrates the potential of the technique for treating cartilage defects caused either by trauma or disease (such as osteoarthritis). Switching stem cells to generate cartilage *in vivo* via remote magnetic particle activation allows sites of degeneration to be repaired.
3. Based on these studies, I believe that one of skill in the art could reasonably employ the techniques disclosed in the instant patent application to regenerate tissue by associating magnetizable particles with one or more ion channels of a ligamentum cell, tenocyte, chondrocyte or stromal cell and manipulating the ion channel(s) using a magnetic field.
4. The undersigned further declares that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful, false statements, and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 35 of the United States Code.

Serial no. 10/518,956  
Declaration of Professor El Haj



Professor Alicia El Haj  
Institute Director

11<sup>th</sup> December 2008

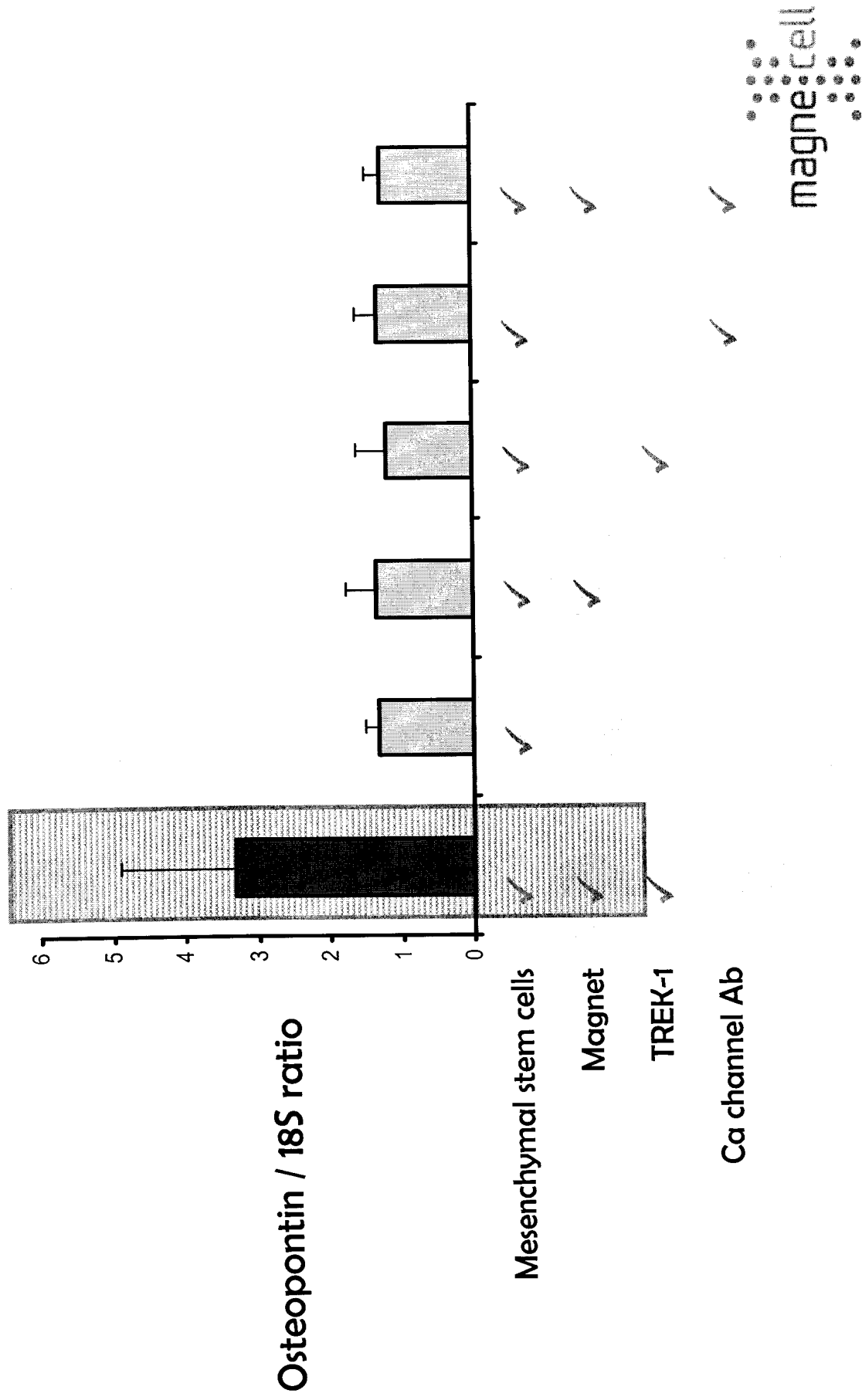
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Alicia Jennifer Hafeeza El Haj

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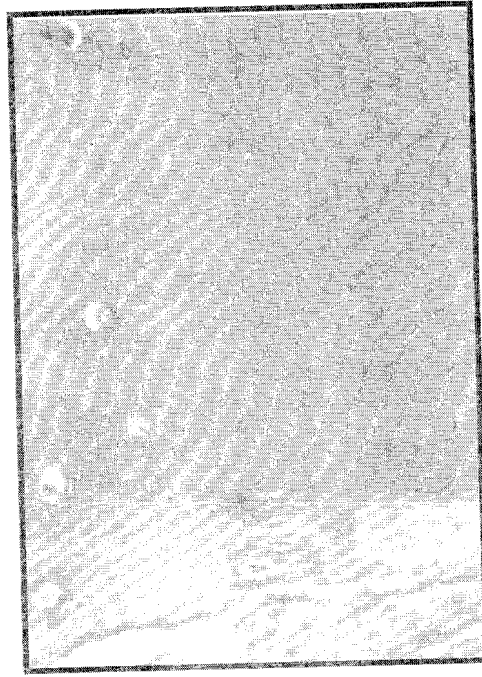
Date

# Exhibit A: TREK activation in vitro



## Exhibit B:

### TREK activation *in vivo*: Cartilage growth



**Control:**  
No cartilage growth



**Active:**  
Evident cartilage growth